

2-ethylhexyl palmitate or a blend of branched chain esters may be used. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils can be used.

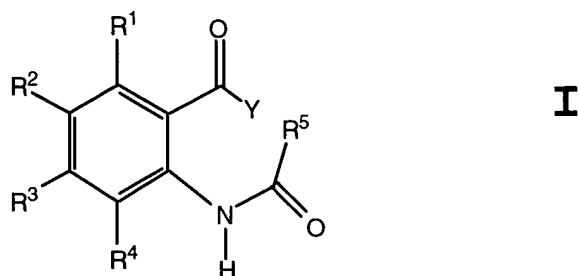
5 Formulations suitable for topical administration to the eye also include eye drops wherein the active ingredients are dissolved or suspended in suitable carrier, especially an aqueous solvent for the active ingredients. The antiviral active ingredients are preferably present in such formulations in a concentration of 0.5 to 20%, advantageously 0.5 to 10% and particularly about 1.5% w/w.

10 Although this invention has been described with respect to specific embodiments, the details of these embodiments are not to be construed as limitations.

What is claimed is:

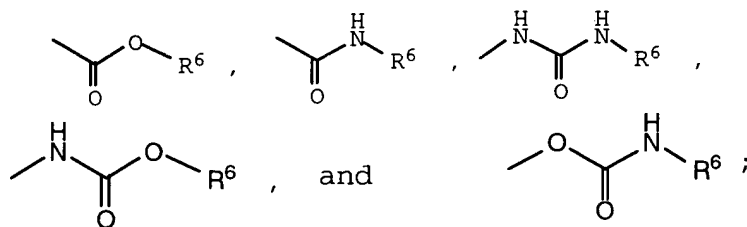
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1. A compound of Formula I



20 wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, alkyl, aralkyl, halo, alkoxy, cyano, nitro, amino, alkylamino, N-acylamino, alkylsulfonyloxy, aminosulfonyl, N-(haloalkylcarbonyl)amino, peptidyl, amino acid residue,

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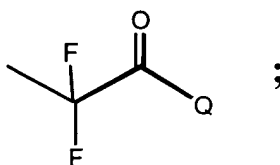
wherein R<sup>5</sup> is selected from alkoxy, aryloxy, aralkyloxy, alkylthio, arylthio, aralkylthio, alkylamino, arylamino, aralkylamino, alkyl, aryl, aralkyl,

heterocyclyl, and heterocyclylalkyl, wherein  $R^5$  is optionally substituted at a substitutable position with one or more substituents selected from alkyl, alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino, alkoxycarbonyl, amino acid residue and peptidyl;

5 wherein  $R^6$  is selected from alkyl, aryl, aralkyl, heterocyclyl and heterocyclylalkyl, wherein  $R^6$  is optionally substituted at a substitutable position with a radical selected from alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino and alkoxycarbonyl;

wherein Y is selected from fluoroalkyl and

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wherein Q is selected from alkoxy, aryloxy, aralkyloxy, amino acid residue, peptidyl, and  $-NHR^7$ ; and

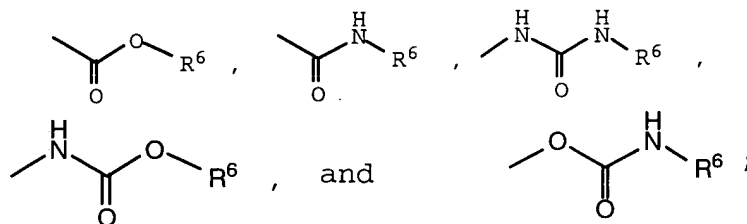
15 wherein  $R^7$  is a radical selected from alkyl, aralkyl, and heterocyclylalkyl, wherein  $R^7$  is optionally substituted at a substitutable position with a radical selected from amino, nitrogen-containing heterocyclyl and alkylamino;

or a pharmaceutically-acceptable salt or tautomer thereof.

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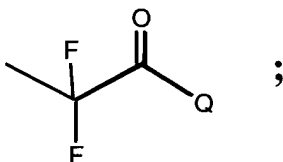
2. Compound of Claim 1 wherein each of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  is independently selected from hydrido, lower alkyl, lower aralkyl, halo, lower alkoxy, cyano, nitro, amino, lower alkylamino, N-acylamino, lower alkylsulfonyloxy, aminosulfonyl, lower N-(haloalkylcarbonyl)amino, amino acid residue, peptidyl,

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30 wherein  $R^5$  is selected from lower alkoxy, phenyloxy, lower aralkyloxy, lower alkylthio, phenylthio, lower aralkylthio, lower alkylamino, arylamino, lower

- aralkylamino, lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocyclyl, and lower heterocyclylalkyl, wherein  $R^5$  is optionally substituted at a substitutable position with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxy carbonyl, amino acid residue and peptidyl; wherein  $R^6$  is selected from lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocyclyl and lower heterocyclylalkyl, wherein  $R^6$  is optionally substituted at a substitutable position with a radical selected from lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, and lower alkoxy carbonyl; wherein Y is selected from lower fluoroalkyl and

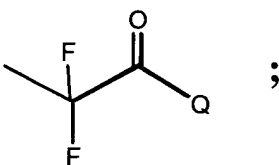


- wherein Q is selected from lower alkoxy, phenyloxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and  $-NHR^7$ ; and wherein  $R^7$  is a radical selected from lower alkyl, lower aralkyl, and lower heterocyclylalkyl, wherein  $R^7$  is optionally substituted at a substitutable position with one or more radical selected from amino, 5-6-membered nitrogen-containing heterocyclyl and lower N,N-dialkylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

3. Compound of Claim 2 wherein Y is lower fluoroalkyl; wherein each of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein  $R^5$  is selected from phenylalkoxy, lower alkyl substituted with halo or phenyloxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein  $R^5$  is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxy carbonyl, amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

4. Compound of Claim 3 wherein Y is selected from difluoromethyl, trifluoromethyl, pentafluoroethyl, heptafluoropropyl, 1,1-difluoroethyl, and 1,1-difluoropropyl; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; wherein R<sup>5</sup> is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl, phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R<sup>5</sup> is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

5. Compound of Claim 2 wherein Y is



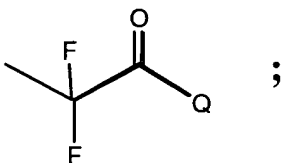
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- wherein Q is selected from lower alkoxy, phenyloxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and -NHR<sup>7</sup>; and wherein R<sup>7</sup> is a radical selected from lower alkyl, lower aralkyl, and lower heteroaralkyl, wherein R<sup>7</sup> is optionally substituted at a substitutable position with a radical selected from amino, 5-6 membered nitrogen-containing heterocyclyl and lower N,N-dialkylamino; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R<sup>5</sup> is selected from phenylalkoxy, lower alkyl

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substituted with halo or phenoxy, phenyl, lower phenylalkyl, and five-ten  
 membered heteroaryl, wherein  $R^5$  is optionally substituted at a  
 substitutable position of a phenyl or heteroaryl radical with one or more  
 substituents selected from lower alkyl, lower alkoxy, phenoxy, lower  
 5 alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino,  
 lower alkoxy carbonyl, amino acid residue, and peptidyl; or a  
 pharmaceutically-acceptable salt or tautomer thereof.

6. Compound of Claim 5 wherein Y is

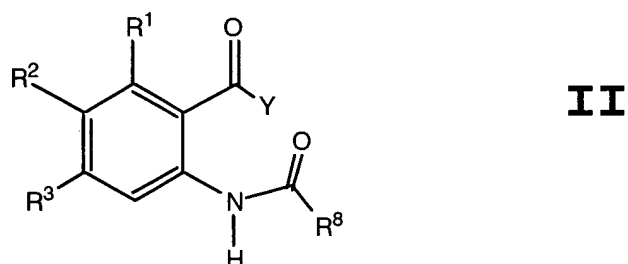


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wherein Q is selected from methoxy, ethoxy, propoxy, isopropoxy, butoxy,  
 phenoxy, benzyloxy, phenylethoxy, and  $-NHR^7$ ; and wherein  $R^7$  is a  
 radical selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl,  
 15 sec-butyl, *tert*-butyl, pentyl, hexyl, benzyl, phenethyl, oxazolylmethyl,  
 oxazolyloethyl, imidazolylmethyl, imidazolylethyl, oxazolinylmethyl,  
 oxazolinylethyl, indolylethyl, indolylmethyl, pyridylmethyl, thienylmethyl,  
 and furylethyl, wherein  $R^7$  is optionally substituted at a substitutable  
 position with a radical selected from amino, piperidinyl, piperazinyl,  
 20 pyrrolidinyl, morpholinyl, pyridyl, pyrimidyl and N,N-dimethylamino;  
 wherein each of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  is independently selected from hydrido,  
 methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl,  
 pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy,  
 isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; and wherein  $R^5$  is  
 25 selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl,  
 difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl,  
 pentafluoroethyl, heptafluoropropyl, difluorochloromethyl,  
 dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl,  
 dichloropropyl, phenoxyethyl, phenoxypropyl, phenyl, phenylmethyl,  
 30 phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl,  
 benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein  $R^5$  is optionally  
 substituted at a substitutable position on a phenyl or heteroaryl radical with  
 one or more substituents selected from methyl, ethyl, n-propyl, isopropyl,  
 n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy,

propoxy, isopropoxy, butoxy, *tert*-butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, N-acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

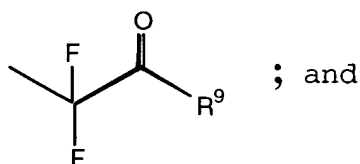
## 7. A compound of Formula II



5            wherein each of R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> is independently selected from hydrido, halo, and nitro;

             wherein R<sup>8</sup> is selected from haloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted arylalkoxy and optionally substituted aryloxyalkyl;

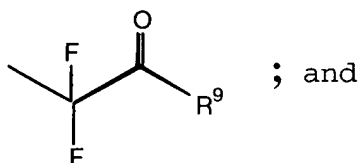
10           wherein Y is selected from fluoroalkyl, and



             wherein R<sup>9</sup> is alkylamino;

15           or a pharmaceutically-acceptable salt or tautomer thereof.

8. Compound of Claim 7 wherein R<sup>1</sup> is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R<sup>2</sup> is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R<sup>3</sup> is selected from hydrido, fluoro, chloro, bromo, iodo and nitro; wherein R<sup>8</sup> is selected from trifluoromethyl, phenyl, phenylmethyl, phenylethyl, furyl, pyridyl, pyrazinyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, phenylmethoxy, (phenyloxy)propyl and phenyloxymethyl; wherein Y is selected from trifluoromethyl and

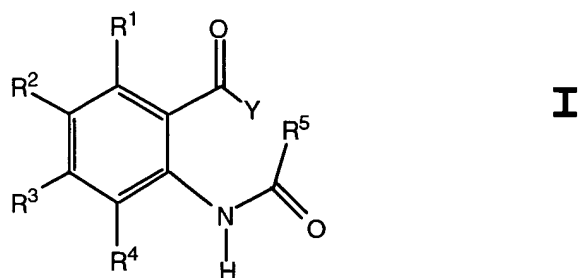


wherein R<sup>9</sup> is selected from methylamino, ethylamino, propylamino, isopropylamino and N,N-dimethylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

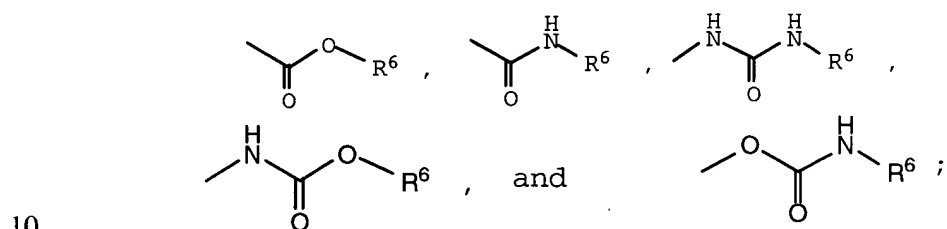
- 5           9. Compound of Claim 8 selected from compounds and their pharmaceutically-acceptable salts, of the group consisting of

10           ?-phenoxy-N-[2-(2,2,2-trifluoro-1-oxo-ethyl)phenyl]butanamide;  
               N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
               N-[5-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
               N-[3-chloro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
               N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
 15           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyrazine-2-carboxamide;  
               phenylmethyl N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]carbamate;  
               N-[5-nitro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
               N-[4-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-  
 20           carboxamide;  
               N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]-1-benzothiophene-2-carboxamide;  
               ?,?,?-trifluoro-N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]acetamide;  
               N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyridine-2-carboxamide;  
 25           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]2-methoxybenzamide;  
               N-[4-iodo-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
               N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]4-chlorophenoxyacetamide;  
               N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]indolyl-2-carboxamide;  
 30           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzofuranyl-2-carboxamide; and  
               N-[2-(3-(2-propylamino)-3-oxo-2,2-difluoro-1-oxopropyl)phenyl]2-methoxyphenylcarboxamide.

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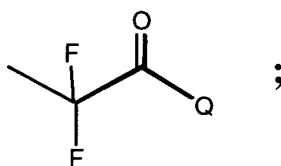
wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from  
 5 hydrido, alkyl, aralkyl, halo, alkoxy, cyano, nitro, amino, alkylamino, N-  
 acylamino, alkylsulfonyloxy, aminosulfonyl, N-(haloalkylcarbonyl)amino,  
 peptidyl, amino acid residue,



wherein R<sup>5</sup> is selected from alkoxy, aryloxy, aralkyloxy, alkylthio,  
 arylthio, aralkylthio, alkylamino, arylamino, aralkylamino, alkyl, aryl, aralkyl,  
 heterocyclyl, and heterocyclylalkyl, wherein R<sup>5</sup> is optionally substituted at a  
 15 substitutable position with one or more substituents selected from alkyl, alkoxy,  
 aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino,  
 alkoxycarbonyl, amino acid residue and peptidyl;

wherein R<sup>6</sup> is selected from alkyl, aryl, aralkyl, heterocyclyl and  
 heterocyclylalkyl, wherein R<sup>6</sup> is optionally substituted at a substitutable position  
 20 with a radical selected from alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-  
 acylamino, amino, alkylamino and alkoxycarbonyl;

wherein Y is selected from fluoroalkyl and

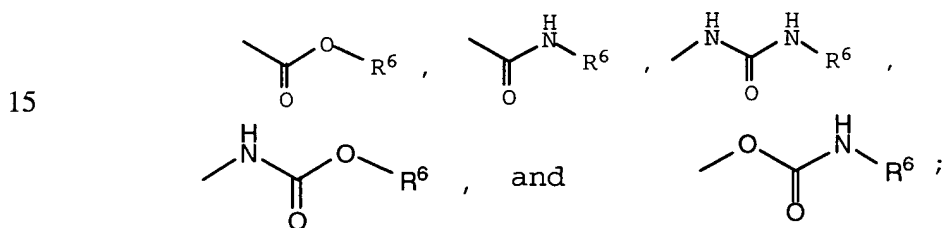


wherein Q is selected from alkoxy, aryloxy, aralkyloxy, amino acid residue, peptidyl, and  $\text{-NHR}^7$ ; and

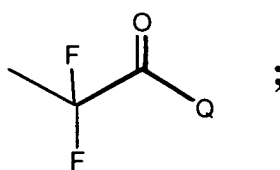
wherein  $\text{R}^7$  is a radical selected from alkyl, aralkyl, and heterocyclalkyl, wherein  $\text{R}^7$  is optionally substituted at a substitutable position with a radical selected from amino, nitrogen-containing heterocycl and alkylamino;

or a pharmaceutically-acceptable salt or tautomer thereof.

11. A pharmaceutical composition of Claim 10 wherein each of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  is independently selected from hydrido, lower alkyl, lower aralkyl, halo, lower alkoxy, cyano, nitro, amino, lower alkylamino, N-acylamino, lower alkylsulfonyloxy, aminosulfonyl, lower N-(haloalkylcarbonyl)amino, amino acid residue, peptidyl,



- wherein  $\text{R}^5$  is selected from lower alkoxy, phenyloxy, lower aralkyloxy, lower alkylthio, phenylthio, lower aralkylthio, lower alkylamino, arylamino, lower aralkylamino, lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl, and lower heterocyclalkyl, wherein  $\text{R}^5$  is optionally substituted at a substitutable position with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxy, amino acid residue and peptidyl; wherein  $\text{R}^6$  is selected from lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl and lower heterocyclalkyl, wherein  $\text{R}^6$  is optionally substituted at a substitutable position with a radical selected from lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, and lower alkoxy; wherein Y is selected from lower fluoroalkyl and



wherein Q is selected from lower alkoxy, phenyloxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and -NHR<sup>7</sup>; and wherein R<sup>7</sup> is a radical  
 5 selected from lower alkyl, lower aralkyl, and lower heterocyclalkyl, wherein R<sup>7</sup> is optionally substituted at a substitutable position with one or more radical selected from amino, 5-6-membered nitrogen-containing heterocycl and lower N,N-dialkylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

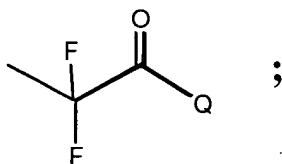
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12. A pharmaceutical composition of Claim 11 wherein Y is lower fluoroalkyl; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R<sup>5</sup> is selected from phenylalkoxy, lower alkyl substituted with  
 15 halo or phenyloxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein R<sup>5</sup> is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxycarbonyl,  
 20 amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

13. A pharmaceutical composition of Claim 12 wherein Y is selected from difluoromethyl, trifluoromethyl, pentafluoroethyl,  
 25 heptafluoropropyl, 1,1-difluoroethyl, and 1,1-difluoropropyl; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; wherein R<sup>5</sup> is selected from  
 30 phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl,

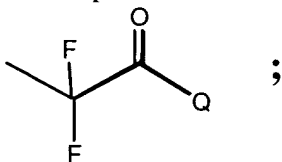
phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein  $R^5$  is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

14. A pharmaceutical composition of Claim 11 wherein Y is



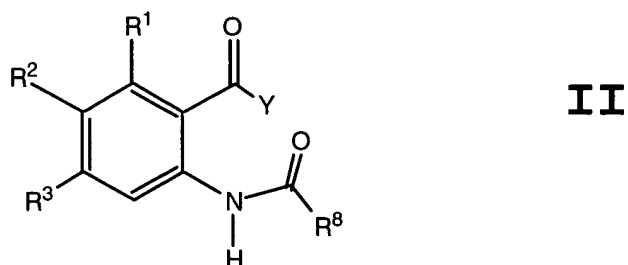
wherein Q is selected from lower alkoxy, phenyloxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and  $-NHR^7$ ; and wherein  $R^7$  is a radical selected from lower alkyl, lower aralkyl, and lower heteroaralkyl, wherein  $R^7$  is optionally substituted at a substitutable position with a radical selected from amino, 5-6 membered nitrogen-containing heterocyclyl and lower N,N-dialkylamino; wherein each of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein  $R^5$  is selected from phenylalkoxy, lower alkyl substituted with halo or phenyloxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein  $R^5$  is optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxy carbonyl, amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

15. A pharmaceutical composition of Claim 14 wherein Y is



wherein Q is selected from methoxy, ethoxy, propoxy, isopropoxy, butoxy, phenyloxy, benzyloxy, phenylethoxy, and -NHR<sup>7</sup>; and wherein R<sup>7</sup> is a radical selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, benzyl, phenethyl, oxazolylmethyl, oxazolylethyl, imidazolylmethyl, imidazolylethyl, oxazolinylmethyl, oxazolinylethyl, indolylethyl, indolylmethyl, pyridylmethyl, thienylmethyl, and furylethyl, wherein R<sup>7</sup> is optionally substituted at a substitutable position with a radical selected from amino, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, pyridyl, pyrimidyl and N,N-dimethylamino; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; and wherein R<sup>5</sup> is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl, phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R<sup>5</sup> is optionally substituted at a substitutable position on a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, N-acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

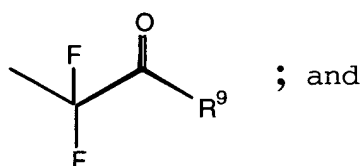
16. A pharmaceutical composition comprising a therapeutically-effective amount of a compound and a pharmaceutically-acceptable carrier or diluent, said compound selected from a compound of Formula II



wherein each of  $R^1$ ,  $R^2$ , and  $R^3$  is independently selected from hydrido, halo, and nitro;

- 5        wherein  $R^8$  is selected from haloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted arylalkoxy and optionally substituted aryloxyalkyl;

wherein Y is selected from fluoroalkyl, and

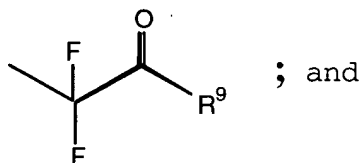


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wherein  $R^9$  is alkylamino;

or a pharmaceutically-acceptable salt or tautomer thereof.

- 15        17. A pharmaceutical composition of Claim 16 wherein  $R^1$  is selected from hydrido, fluoro, chloro, bromo and iodo; wherein  $R^2$  is selected from hydrido, fluoro, chloro, bromo and iodo; wherein  $R^3$  is selected from hydrido, fluoro, chloro, bromo, iodo and nitro; wherein  $R^8$  is selected from trifluoromethyl, phenyl, phenylmethyl, phenylethyl, furyl, pyridyl, pyrazinyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, phenylmethoxy, (phenoxy)propyl and phenyloxymethyl; wherein Y is selected from trifluoromethyl and
- 20

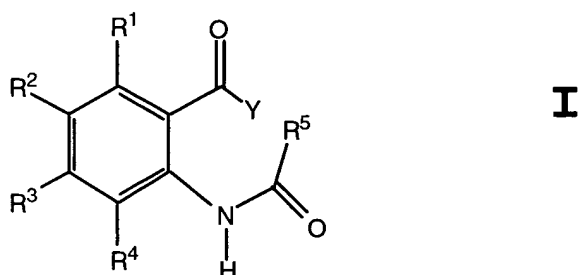


25

wherein R<sup>9</sup> is selected from methylamino, ethylamino, propylamino, isopropylamino and N,N-dimethylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

- 5           18. A pharmaceutical composition of Claim 17 wherein the compound is selected from compounds and their pharmaceutically-acceptable salts, of the group consisting of
- 10           ?-phenoxy-N-[2-(2,2,2-trifluoro-1-oxo-ethyl)phenyl]butanamide;  
           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
           N-[5-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
           N-[3-chloro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
 15           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyrazine-2-carboxamide;  
           phenylmethyl N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]carbamate;  
           N-[5-nitro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
 20           N-[4-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]-1-benzothiophene-2-carboxamide;  
           ?,?,?-trifluoro-N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]acetamide;  
 25           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyridine-2-carboxamide;  
           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]2-methoxybenzamide;  
           N-[4-iodo-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]4-chlorophenoxyacetamide;  
 30           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]indolyl-2-carboxamide;  
           N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzofuranyl-2-carboxamide; and  
           N-[2-(3-(2-propylamino)-3-oxo-2,2-difluoro-1-oxopropyl)phenyl]2-methoxyphenylcarboxamide.

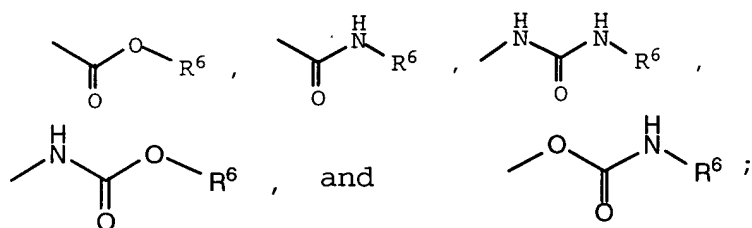
19. A method of treating herpes viral infection in a subject, said method comprising treating said subject with an effective amount of a compound of Formula I



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wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, alkyl, aralkyl, halo, alkoxy, cyano, nitro, amino, alkylamino, N-acylamino, alkylsulfonyloxy, aminosulfonyl, N-(haloalkylcarbonyl)amino, peptidyl, amino acid residue,

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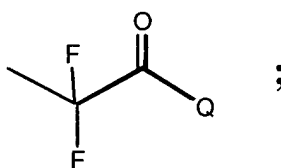
15 wherein R<sup>5</sup> is selected from alkoxy, aryloxy, aralkyloxy, alkylthio, arylthio, aralkylthio, alkylamino, arylamino, aralkylamino, alkyl, aryl, aralkyl, heterocyclyl, and heterocyclylalkyl, wherein R<sup>5</sup> is optionally substituted at a substitutable position with one or more substituents selected from alkyl, alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino, alkoxy carbonyl, amino acid residue and peptidyl;

20

wherein R<sup>6</sup> is selected from alkyl, aryl, aralkyl, heterocyclyl and heterocyclylalkyl, wherein R<sup>6</sup> is optionally substituted at a substitutable position with a radical selected from alkoxy, aryloxy, alkylthio, arylthio, halo, nitro, N-acylamino, amino, alkylamino and alkoxy carbonyl;

25

wherein Y is selected from fluoroalkyl and



wherein Q is selected from alkoxy, aryloxy, aralkyloxy, amino acid residue, peptidyl, and -NHR<sup>7</sup>; and

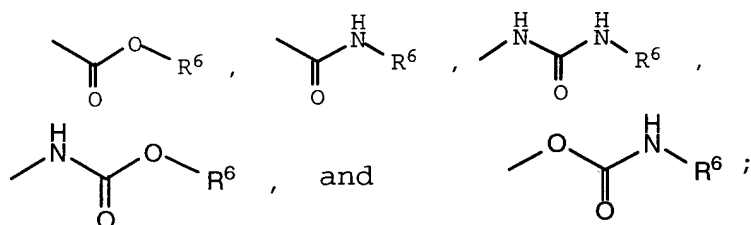
- 5        wherein R<sup>7</sup> is a radical selected from alkyl, aralkyl, and heterocyclalkyl, wherein R<sup>7</sup> is optionally substituted at a substitutable position with a radical selected from amino, nitrogen-containing heterocycl and alkylamino;  
       or a pharmaceutically-acceptable salt or tautomer thereof.

10

20. A method of Claim 19 wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, lower alkyl, lower aralkyl, halo, lower alkoxy, cyano, nitro, amino, lower alkylamino, N-acylamino, lower alkylsulfonyloxy, aminosulfonyl, lower N-(haloalkylcarbonyl)amino, amino acid

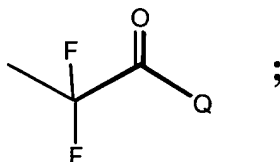
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residue, peptidyl,



- 20        wherein R<sup>5</sup> is selected from lower alkoxy, phenyloxy, lower aralkyloxy, lower alkylthio, phenylthio, lower aralkylthio, lower alkylamino, arylamino, lower aralkylamino, lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl, and lower heterocyclalkyl, wherein R<sup>5</sup> is optionally substituted at a substitutable position with one or more substituents selected from lower
- 25        alkyl, lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxy carbonyl, amino acid residue and peptidyl; wherein R<sup>6</sup> is selected from lower alkyl, 6-10-membered aryl, lower aralkyl, 5-10-membered heterocycl and lower heterocyclalkyl, wherein R<sup>6</sup> is optionally substituted at a substitutable position with a radical
- 30        selected from lower alkoxy, phenyloxy, lower alkylthio, phenylthio, halo, nitro,

N-acylamino, amino, lower alkylamino, and lower alkoxy carbonyl; wherein Y is selected from lower fluoroalkyl and



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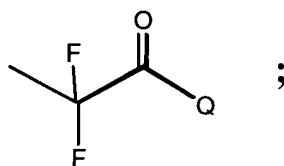
wherein Q is selected from lower alkoxy, phenoxy, lower aralkyloxy, N-amino acid residue, N-peptidyl, and -NHR<sup>7</sup>; and wherein R<sup>7</sup> is a radical selected from lower alkyl, lower aralkyl, and lower heterocyclalkyl, wherein R<sup>7</sup> is optionally substituted at a substitutable position with one or  
 10 more radical selected from amino, 5-6-membered nitrogen-containing heterocycl and lower N,N-dialkylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

– 21. A method of Claim 20 wherein Y is lower fluoroalkyl; wherein  
 15 each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro, and amino; and wherein R<sup>5</sup> is selected from phenylalkoxy, lower alkyl substituted with halo or phenoxy, phenyl, lower phenylalkyl, and five-ten membered heteroaryl, wherein R<sup>5</sup> is  
 20 optionally substituted at a substitutable position of a phenyl or heteroaryl radical with one or more substituents selected from lower alkyl, lower alkoxy, phenoxy, lower alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino, lower alkoxy carbonyl, amino acid residue, and peptidyl; or a pharmaceutically-acceptable salt or tautomer thereof.

25 22. A method of Claim 21 wherein Y is selected from difluoromethyl, trifluoromethyl, pentafluoroethyl, heptafluoropropyl, 1,1-difluoroethyl, and 1,1-difluoropropyl; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo,  
 30 iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; wherein R<sup>5</sup> is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl,

difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl,  
 phenoxyethyl, phenoxypropyl, phenyl, phenylmethyl, phenylethyl,  
 furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl,  
 benzofuranyl, indolyl, and pyridyl, wherein R<sup>5</sup> is optionally substituted at a  
 5 substitutable position of a phenyl or heteroaryl radical with one or more  
 substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl,  
 isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy,  
 isopropoxy, butoxy, *tert*-butoxy, phenoxy, methylthio, phenylthio, fluoro,  
 chloro, bromo, iodo, nitro, N-formylamino, acetylamino, amino, N,N-  
 10 dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable  
 salt or tautomer thereof.

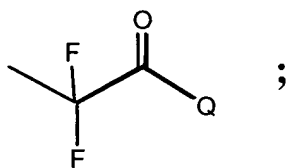
23. A method of Claim 20 wherein Y is



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wherein Q is selected from lower alkoxy, phenoxy, lower aralkyloxy, N-  
 amino acid residue, N-peptidyl, and -NHR<sup>7</sup>; and wherein R<sup>7</sup> is a radical  
 selected from lower alkyl, lower aralkyl, and lower heteroaralkyl, wherein  
 20 R<sup>7</sup> is optionally substituted at a substitutable position with a radical  
 selected from amino, 5-6 membered nitrogen-containing heterocyclyl and  
 lower N,N-dialkylamino; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is  
 independently selected from hydrido, lower alkyl, halo, lower alkoxy, nitro,  
 and amino; and wherein R<sup>5</sup> is selected from phenylalkoxy, lower alkyl  
 25 substituted with halo or phenoxy, phenyl, lower phenylalkyl, and five-ten  
 membered heteroaryl, wherein R<sup>5</sup> is optionally substituted at a  
 substitutable position of a phenyl or heteroaryl radical with one or more  
 substituents selected from lower alkyl, lower alkoxy, phenoxy, lower  
 alkylthio, phenylthio, halo, nitro, N-acylamino, amino, lower alkylamino,  
 30 lower alkoxycarbonyl, amino acid residue, and peptidyl; or a  
 pharmaceutically-acceptable salt or tautomer thereof.

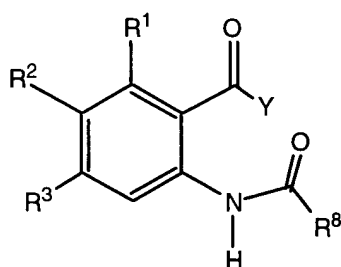
24. A method of Claim 23 wherein Y is



wherein Q is selected from methoxy, ethoxy, propoxy, isopropoxy, butoxy, phenyloxy, benzyloxy, phenylethoxy, and -NHR<sup>7</sup>; and wherein R<sup>7</sup> is a radical selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, benzyl, phenethyl, oxazolymethyl, oxazolyloethyl, imidazolymethyl, imidazolylethyl, oxazolinylmethyl, oxazolinylethyl, indolylethyl, indolylmethyl, pyridylmethyl, thienylmethyl, and furylethyl, wherein R<sup>7</sup> is optionally substituted at a substitutable position with a radical selected from amino, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, pyridyl, pyrimidyl and N,N-dimethylamino; wherein each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, fluoro, chloro, bromo, iodo, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, nitro, and amino; and wherein R<sup>5</sup> is selected from phenylmethoxy, phenylethoxy, phenylpropoxy, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, phenyloxyethyl, phenyloxypropyl, phenyl, phenylmethyl, phenylethyl, furyl, pyrazinyl, oxazolyl, thiazolyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, and pyridyl, wherein R<sup>5</sup> is optionally substituted at a substitutable position on a phenyl or heteroaryl radical with one or more substituents selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, hexyl, methoxy, ethoxy, propoxy, isopropoxy, butoxy, *tert*-butoxy, *tert*-butoxy, phenyloxy, methylthio, phenylthio, fluoro, chloro, bromo, iodo, nitro, N-formylamino, N-acetylamino, amino, N,N-dimethylamino and methoxycarbonyl; or a pharmaceutically-acceptable salt or tautomer thereof.

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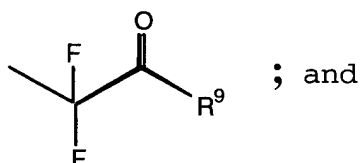
25. A method of treating herpes viral infection in a subject, said method comprising treating said subject with an effective amount of a compound of Formula II

**II**

wherein each of R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> is independently selected from hydrido, halo, and nitro;

- 5        wherein R<sup>8</sup> is selected from haloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted arylalkoxy and optionally substituted aryloxyalkyl;

wherein Y is selected from fluoroalkyl, and



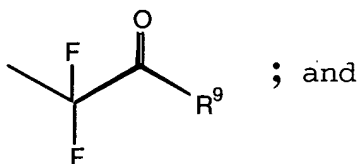
; and

10

wherein R<sup>9</sup> is alkylamino;

or a pharmaceutically-acceptable salt or tautomer thereof.

- 15        26. A method of Claim 25 wherein R<sup>1</sup> is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R<sup>2</sup> is selected from hydrido, fluoro, chloro, bromo and iodo; wherein R<sup>3</sup> is selected from hydrido, fluoro, chloro, bromo, iodo and nitro; wherein R<sup>8</sup> is selected from trifluoromethyl, phenyl, phenylmethyl, phenylethyl, furyl, pyridyl, pyrazinyl, thienyl, pyrrolyl, benzothienyl, benzofuranyl, indolyl, phenylmethoxy, (phenyloxy)propyl and
- 20        phenyloxymethyl; wherein Y is selected from trifluoromethyl and



; and

- 25        wherein R<sup>9</sup> is selected from methylamino, ethylamino, propylamino, isopropylamino and N,N-dimethylamino; or a pharmaceutically-acceptable salt or tautomer thereof.

27. A method of Claim 26 wherein the compound is selected from compounds and their pharmaceutically-acceptable salts, of the group consisting of

- 5            ?-phenoxy-N-[2-(2,2,2-trifluoro-1-oxo-ethyl)phenyl]butanamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
          N-[5-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
10          N-[3-chloro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyrazine-2-carboxamide;  
          phenylmethyl N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]carbamate;  
15          N-[5-nitro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzenepropanamide;  
          N-[4-fluoro-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]-1-benzothiophene-2-carboxamide;  
20          ?,?,?-trifluoro-N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]acetamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]pyridine-2-carboxamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]2-methoxybenzamide;  
          N-[4-iodo-2-(2,2,2-trifluoro-1-oxoethyl)phenyl]furan-2-carboxamide;  
25          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]4-chlorophenoxyacetamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]indolyl-2-carboxamide;  
          N-[2-(2,2,2-trifluoro-1-oxoethyl)phenyl]benzofuranyl-2-carboxamide; and  
30          N-[2-(3-(2-propylamino)-3-oxo-2,2-difluoro-1-oxopropyl)phenyl]2-methoxyphenylcarboxamide.

28.       The method of Claim 19 wherein the subject is infected with a herpesvirus selected from herpes simplex virus type-1 (HSV-1), herpes  
35       simplex virus type-2 (HSV-2), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus, herpesvirus-6 (HHV-6), herpesvirus-7 (HHV-7), herpesvirus-8 (HHV-8), pseudorabies and rhinotracheitis.

29. A method of inhibiting a viral protease, said method comprising treating said subject with an effective amount of a compound of Claim 1.

5           30. Method of Claim 19 wherein the viral protease is a herpesvirus protease.

          31. Method of Claim 30 wherein the viral protease is selected from a CMV protease, an HSV-1 protease and a HSV-2 protease.  
10

          32. Method of Claim 31 wherein the viral protease is a CMV protease, encoded by U<sub>L</sub>80.

          33. A method of prophylactic treatment of herpes viral infection  
15 in a subject, said method comprising treating said subject with an effective amount of a compound of Claim 1.

          34. The method of Claim 33 wherein the herpesvirus is selected from herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2  
20 (HSV-2), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus, herpesvirus-6 (HHV-6), herpesvirus-7 (HHV-7), herpesvirus-8 (HHV-8), pseudorabies and rhinotracheitis.

## 25           ELECTROPHILIC KETONES FOR THE TREATMENT OF HERPESVIRUS INFECTIONS

### ABSTRACT

30           A class of compounds is described which can be used for the treatment of viral infections. Compounds of particular interest are defined by Formula II